REMARKS

Claims 1, 2, 7-12, 14-24 and 27-41 will be pending in this application upon entry of the foregoing amendments. Claims 1 and 27 are the only independent claims.

Claims 1 and 27 have been amended without prejudice. The amendments are supported by the Specification and claims as originally filed. For example, support for the amendments is found at least from original claim 3.

Claim 3 is cancelled without prejudice to avoid redundancy with the amended claim 1.

The foregoing amendments do not add any new matter to the application. The amendments and the arguments presented below raise no new issues that would require further consideration and/or search. Thus, entry of the Amendment after the Final Rejection is respectfully requested.

Claim rejections – 35 U.S.C. § 103

Claims 1-3, 7-9, 11, 12, 14-24 and 27-41 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2003/0107149 ("'149 application") in view of U.S. Patent No. 6,099,683 ("'863 patent").

The Examiner states that "it would have been obvious to include the galanthamine salt of the '863 patent into the thin oral films of the '149 patent [*sic,* application] since the '149 reference is suggestive of cholinesterase inhibitors and discloses fast dissolving oral dosage forms." The Examiner continues that the "combination would have been obvious following the suggestions of the '149 application and teachings of the '863 [patent] to quickly deliver the compounds orally." The Examiner states that "since the same compounds must have the same features and function, the thin film of the prior art combination that comprise a galanthamine compound and a polymer *inherently* will dissolve within 30 minutes and achieved an optimal plasma concentration." The Examiner also refers to Example 6 of the '863 patent, stating that the "formulations dissolve in the *oral cavity* and begin to deliver their active payloads within 5 minutes."

Applicants respectfully disagree and submit that claims 1 and 27 and their dependent claims 2, 7-9, 11, 12, 14-24 and 28-41 are patentable in view of the cited prior art references at

least because: (1) the prior art did not teach or suggest a film-shaped medicament for buccal administration of galanthamine or a salt or derivative thereof, to achieve an effective plasma level of galanthamine or the salt or derivative thereof within thirty minutes after the buccal administration; (2) the presently claimed film-shaped medicament has achieved superior results, i.e., it achieved the desired effects on the central nervous system within a short time, but without unacceptable peripheral side effects; and (3) the superior results could not have been reasonably predicted based on the '149 application's general disclosure on using thin films for delivery of cholinesterase inhibitors and the '863 patent's disclosure on fast-dissolving galanthamine hydrobromide tablet.

Applicants respectfully point out that none of the cited prior art teaches or suggests a film-shaped formulation of galanthamine that will ***inherently*** dissolve within 30 minutes and achieve an optimal plasma concentration as suggested by the Examiner. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). See MPEP 2112.

The dissolution profile recited in the present claims 1 and 27 does not necessarily flow from the teachings of the applied prior art. According to the '149 application, the thin films can have various drug release profiles, e.g., immediate, delayed, sustained or sequential release profiles. See e.g., paragraphs [0090] to [0095]. Nowhere does the '149 application describe a thin film formulation that releases the active ingredient within 30 minutes to achieve an optimal plasma concentration, let alone a thin film formulation for buccal administration of galanthamine to achieve an effective plasma level of galanthamine within thirty minutes after the buccal administration. Example 6 of the '863 patent does not show that "formulations dissolve in the *oral cavity* and begin to deliver their active payloads within 5 minutes" as stated by the Examiner. Example 6 describes *in vitro* dissolution studies of the tablet formulations in purified water, not *in vivo* studies of film-shaped formulations in oral cavity. In addition, it is known to those

skilled in the art that tablets deliver their active ingredient(s) into the blood stream primarily via the gastrointestinal tract, not oral cavity. Accordingly, the *in vitro* dissolution studies of tablets disclosed in Example 6 provided no indication what so ever about the dissolution profile of a film-shaped formulation of galanthamine, let alone the dissolution profile recited in the present claims 1 and 27.

Applicants also respectfully submit that the presently claimed film-shaped formulation for buccal administration of galanthamine has achieved superior results that are unexpected from the prior art teaching. As described in the specification, galanthamine has a relatively short half life in plasma, i.e., approx. 5 hours. It is necessary to administer high dosages in order to maintain the plasma concentration in the therapeutically effective range for as long as possible between dose administrations. This causes markedly high plasma concentration in an uncontrolled manner immediately after oral administration of fast release galanthamine dosage forms, which in some patients, may lead to peripheral, especially gastrointestinal and cardiovascular, side effects. See para. [0013] in the published application. Thus, at the time of the invention, there was an unmet need for a fast release dosage form of galanthamine that affords rapid onset of action without the occurrence of unacceptable peripheral side effects.

None of the cited prior art references discussed the unmet need, let alone providing a solution to meet the need. In view of the known side effect associated with the oral administration of fast release dosage forms of galanthamine, one skilled in the art would have been discouraged from using a rapid release film-shaped formulation for buccal administration of galanthamine, because such formulation would have a faster onset of action in the oral cavity than the tablets that deliver galanthamine to the gastrointestinal tract. An even higher plasma concentration galanthamine, thus more severe side effects, would have been expected from the buccal administration of film-shaped formulation for galanthamine. As stated in the specification:

> In light of the above, it was absolutely to be expected that the use of a rapidly releasing formulation where the onset of action occurs within a few minutes following application would have to involve considerable side effects. Surprisingly, it turned out that it was possible to configure a buccal dosage form in such a way that the active substance shows the desired effects on the central nervous system within a short time, but without unacceptable peripheral side effects having to be accepted. This is

> achieved by providing a formulation of the medicament in the form of a film-shaped medicament for buccal administration.
> *Paragraph [0019] in the published application.*

Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 7-9, 11, 12, 14-24 and 27-41 for being unpatentable over the '149 application in view of the '863 patent are respectfully requested, at least because the combined prior art references did not teach or suggest the claimed invention and the claimed invention has achieved unexpected superior results.

Claims 1-3, 7-12, 14-24 and 27-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over the '149 application in view of the '863 patent, and further in view of U.S. Patent No. 5,904,929 ("Uekama").

As discussed above, the '149 application in view of the '863 patent does not render the presently claimed invention *prima facie* obvious. For reasons similar to those discussed in the Amendment previously submitted on December 28, 2009, Uekama does not compensate for the defects of the '149 application in view of the '863 patent.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 7-9, 11, 12, 14-24 and 27-41 for being unpatentable over the '149 application in view of the '863 patent and further in view of Uekama are respectfully requested.

It is respectfully submitted that the present application, including claims 1, 2, 7-12, 14-24 and 27-41, is in condition for allowance and such action is respectfully solicited. Applicants appreciate the effort of the Examiner and look forward to receiving the Notice of Allowance of all pending claims.

Respectfully submitted,

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